

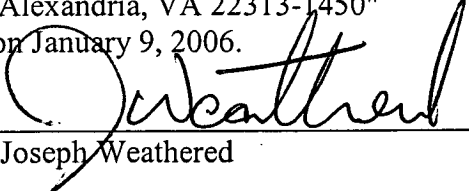


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Joseph Weathered

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

APPLICANT(S) : Larry A. SKLAR et al.
SERIAL NO. : 10/021,243
FILED : 12/19/2001
FOR : Microfluidic Micromixer
GROUP ART UNIT : 1641
EXAMINER : Ann Y. LAM

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BRIEF ON APPEAL

1. REAL PARTY IN INTEREST

The real party of interest in the present application is the University of New Mexico, with an address at Zuni Wing, Rm. 357, Hokona Hall, c/o Patent Administration Office, Albuquerque, New Mexico 87131. The University of New Mexico acquired its interest in the application by virtue of an assignment recorded in the microfiche records of the Patent and Trademark Office at Reel No. 015267, Frame No. 0808 et seq.

2. RELATED APPEALS AND INTERFERENCES

On information and belief, there are no cases currently on appeal before the Board which may have a bearing on the Board's decision in the instant Appeal.

3. STATUS OF CLAIMS

Claims 1-50 are pending in the application. Claims 51-78 have been canceled pursuant to a restriction requirement. Claim 1 is the only independent claim. All of the pending claims stand rejected under 35 U.S.C. § 102(b) or § 103(a).

The appealed claims are set forth in Appendix A.

4. STATUS OF AMENDMENTS

No Amendments were filed after the final Office Action. All Amendments have been entered.

5. SUMMARY OF CLAIMED SUBJECT MATTER

As set forth in independent claim 1, a microfluidic mixing apparatus comprises first driving means for driving a plurality of reagent samples from a plurality of respective source wells into a first fluid flow stream. (Page 2, lines 25-26; page 14, lines 22-24; page 15, lines 24-27) The microfluidic mixing apparatus further comprises second driving means for introducing a separation gas between each of the plurality of reagent samples in the first fluid flow stream to produce a gas-separated first fluid flow stream. (Page 2, lines 27-29; page 15, lines 12-16; page 16, lines 13-17.) Means are provided for driving a second fluid flow stream comprising a plurality of particles (page 14, lines 15-30; page 15, lines 27-31), and a junction device is provided downstream of the first driving

means and the second driving means (page 2, lines 29-30; page 14, lines 22-25; page 15, lines 24-27.). The junction device comprises a first inlet port (page 14, line 25; page 15, line 27) for receiving the gas-separated first fluid flow stream, a second inlet port (page 14, line 30; page 16, line 1) for receiving the second fluid flow stream, a first reaction zone for forcing an initial mixing between the gas-separated first fluid flow stream and the second fluid flow stream to thereby form a reaction product stream (page 15, lines 1-3; page 16, lines 3-5), an outlet port for allowing the reaction product stream to exit the junction device (page 15, line 2; page 16, line 4). (Page 2, line 29, through page 3, line 4.) The microfluidic mixing apparatus further comprises a second reaction zone downstream of the junction device where the plurality of reagent samples and the plurality of particles further mix and form a plurality of reaction products (page 15, lines 2-6; page 16, lines 4-8), the second reaction zone communicating with the outlet port, and means operatively connected to the outlet port and the second reaction zone for selectively analyzing the reaction product stream for the reaction products (page 15, lines 3-10; page 16, lines 5-11).

As set forth in dependent claim 3, the autosampler includes a probe, and the microfluidic mixing apparatus includes a means for exposing a probe tip of the probe to a jet of gas to remove liquid from the probe tip. (page 21, lines 12-14.)

With respect to the means-plus-function recitations in claims 1 and 3, the following citations serve to identify the structures described in the specification as corresponding to the recited functions:

The “first driving means” corresponds in part to autosampler 102 (page 14, line 18; Figure 1) or autosampler 202 (page 15, line 20; Figure 2) and in part to peristaltic pump 114 (page 14, line 24; Figure 1) or peristaltic pump 214 (page 15, line 25; Figure 2).

The “second driving means” likewise corresponds in part to autosampler 102 (page 14, line 18; Figure 1) or autosampler 202 (page 15, line 20; Figure 2) and in part to peristaltic pump 114 (page 14, line 24; Figure 1) or peristaltic pump 214 (page 15, line 25; Figure 2).

The “means for driving a second fluid flow stream” corresponds in part to tube 126 (page 14, lines 27-28; Figure 1) or tube 226 (page 15, lines 29-30; Figure 2) and in part to peristaltic pump 114 (page 14, line 24; Figure 1) or peristaltic pump 214 (page 15, line 25; Figure 2).

The “means ... for selectively analyzing said reaction product stream for said reaction products” corresponds to a flow cytometer including a flow cell 146 or 246 and a laser interrogation device (page 15, lines 7-10; Figure 1)(page 16, lines 8-11; Figure 2).

The “means for exposing a probe tip of said probe to a jet of gas to remove liquid from said probe tip” includes the autosampler 102 or 202 (page 14, line 18; Figure 1)(page 15, line 20; Figure 2).

6. GROUNDS FOR REJECTION TO BE REVIEWED ON APPEAL

Claims 1, 16-18, 21, 24, 29-34, 42-44, 46, 47, 49, and 50 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 2,933,293 to Ferrari, Jr. (“Ferrari”).

Claims 27 and 28 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari.

Claims 19, 20, 22, 23, 25, 26, and 35-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari in view of U.S. Patent No. 6,132,685 to Keresco et al.

Claim 45 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari in view of U.S. Patent No. 6,440,645 to Yon-Hin et al..

Claim 48 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari in view of U.S. Patent No. 6,235, 685 to Knapp et al.

Claims 2-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari in view of U.S. Patent No. 4,853,336 to Saros et al.

Claims 40 and 41 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari in view of U.S. Patent No. 5,679,310 to Manns.

7. ARGUMENT

A. Rejection of Independent Claim 1 Under 35 U.S.C. §102(b)

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 2,933,293 to Ferrari, Jr. ("Ferrari").

Appellants traverse the rejection of independent claim 1 under § 102(b) and maintain that claim 1 distinguishes the invention over the prior art and particularly over Ferrari. Applicants' microfluidic mixing apparatus as defined in amended claim 1 bears only a spurious resemblance to the mixing device of Ferrari.

As set forth in claim 1, a microfluidic mixing apparatus comprises first driving means for driving a plurality of reagent samples from a plurality of respective source wells into a first fluid flow stream, second driving means for introducing a separation gas between each of the plurality of reagent samples in the first fluid flow stream to produce a gas-separated first fluid flow stream, means for driving a second fluid flow stream comprising a plurality of particles,

and a junction device downstream of the first driving means and the second driving means. The junction device comprises a first inlet port for receiving the gas-separated first fluid flow stream, a second inlet port for receiving the second fluid flow stream, a first reaction zone for forcing an initial mixing between the gas-separated first fluid flow stream and the second fluid flow stream to thereby form a reaction product stream, an outlet port for allowing the reaction product stream to exit the junction device. The microfluidic mixing apparatus further comprises a second reaction zone downstream of the junction device where the plurality of reagent samples and the plurality of particles further mix and form a plurality of reaction products, the second reaction zone communicating with the outlet port, and means operatively connected to the outlet port and the second reaction zone for selectively analyzing the reaction product stream for the reaction products.

Ferrari discloses a fluidic circuit that is different from appellants' claimed microfluidic mixing device and that does not suggest appellants' claimed device. Pursuant to the teachings of Ferrari, test samples are combined with a primary processing medium prior to an insertion of air bubbles, as shown in the upper left hand corner of Figure 1. Air-separated samples, already combined with a primary processing medium, are fed to a coil (10) which "acts to thoroughly mix the liquids automatically as they flow therethrough." The mixed gas-separated fluid samples are delivered to a dialyzer (18). The dialyzer also receives air-separated aliquots of a secondary processing medium via a tube (28). These aliquots do not mix in the dialyzer with the air-separated samples from the mixing coil (10). Instead, certain molecular or crystalline components (ions) cross the permeable barrier from one air-separated fluid stream to join the other air-separated fluid stream. The air-separated fluid stream of secondary processing medium from the tube (28), with changes in ionic components, exits

the dialyzer and may be directed to a color development chamber (30). From the color development chamber, the air-separated fluid stream of secondary processing medium passes to a colorimeter (46) via a supply tube (44).

According to appellants' claim 1, a microfluidic mixing apparatus includes a junction device that receives a gas-separated fluid flow sample stream at a first inlet port and a second fluid flow stream at a second inlet port. The gas-separated fluid flow sample stream includes samples from respective reagent source wells. The junction device contains a reaction zone for forcing an initial mixing between the gas-separated first fluid flow stream and the second fluid flow stream to form a reaction product stream.

Pursuant to the teachings of Ferrari, the coil is the only part explicitly designed to force a mixing of incoming fluid components. However, the coil is not a junction device as set forth in appellants' claim 1. The coil of Ferrari has a single inlet port rather than two as set forth in claim 1. The coil does not have one inlet port receiving a gas-separated sample stream and another inlet port receiving a fluid stream of a reagent or processing medium.

The dialyzer (18) of Ferrari has one inlet port (at the top left side of the dialyzer) receiving an air-separated sample stream and another inlet (at the lower left side of the dialyzer) receiving an air-separated stream of secondary processing medium. However, the dialyzer (18) does not permit mixing of the two streams. Instead, there is a limited migration of ionic components across a semi-permeable membrane.

The color development chamber (30) of Ferrari has two inlet ports, but neither of those ports receives a gas-separated sample stream. The samples do not pass through the dialyzer and accordingly cannot arrive at the color development chamber or at the colorimeter (46).

The Examiner contends that the first inlet port and the second inlet port of applicants' junction device have counterparts in the sample inlet and the reagent inlet of Ferrari's pump (12). However, those inlets of Ferrari's device are inlets to the pump and are necessarily upstream thereof. In contrast, in the microfluidic mixing device of applicants' claim 1, the junction device and particularly the inlet ports thereof are downstream of the driving means and receive the gas-separated first fluid flow stream and the second fluid flow stream therefrom.

The Examiner maintains further that the first reaction zone and the second reaction zone of applicants' microfluidic mixing device correspond to reference numerals 30 and 44 in the Ferrari reference, respectively. However, according to appellants' claim 1, the first reaction zone is the situs of initial mixing between the gas-separated first fluid flow stream and the second fluid flow stream to thereby form a reaction product. Such mixing cannot occur at the locations of reference numeral 30 or 44 in the Ferrari fluidic mixing circuit because the gas-separated sample fluid flow stream from the upper part of the Ferrari circuit does not flow to those locations. The gas-separated sample fluid flow stream from the upper part of the Ferrari circuit follows a separate path from that of the reagent flow stream and does not mix therewith. Instead, the gas-separated sample fluid flow stream from the upper part of the Ferrari circuit flows into the upper portion of dialyzer 18 at the left side thereof and flows out of the dialyzer at the upper right port thereof. The gas-separated sample fluid flow stream from the upper part of the Ferrari circuit never flows to locations 30 and 44 in the Ferrari circuit.

B. Rejection of Dependent Claim 3 Under 35 U.S.C. §103(a)

Claim 3 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari in view of U.S. Patent No. 4,853,336 to Saros et al.

Appellants traverse the rejection of claim 3 for the reasons stated above with reference to claim 1. In addition, appellants traverse the rejection of claim 3 for the addition reason that neither Ferrari nor Saros et al. disclose or suggest a means for exposing a probe tip of the autosampler to a jet of gas to remove liquid from the probe tip.

The Saros reference certainly discloses a probe used for aspirating liquid samples. However, Saros et al. say nothing about cleaning the tip of the probe and nothing about directing a jet of gas against the probe.


9. CONCLUSION

In summary, Ferrari does not anticipate claim 1 contrary to the rejection made by the Examiner.

For the foregoing reasons, the rejection of independent claim 1 under 35 U.S.C. § 102(b) is deemed to be improper. Appellant therefore requests that the Examiner be reversed and the application remanded for proceedings towards issuance.

Respectfully submitted,

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APPENDIX: CLAIMS ON APPEAL

1. A microfluidic mixing apparatus comprising:
 - first driving means for driving a plurality of reagent samples from a plurality of respective source wells into a first fluid flow stream;
 - second driving means for introducing a separation gas between each of said plurality of reagent samples in said first fluid flow stream to produce a gas-separated first fluid flow stream;
 - means for driving a second fluid flow stream comprising a plurality of particles;
 - a junction device downstream of said first driving means and said second driving means, said junction device comprising:
 - a first inlet port for receiving said gas-separated first fluid flow stream;
 - a second inlet port for receiving said second fluid flow stream;
 - a first reaction zone for forcing an initial mixing between said gas-separated first fluid flow stream and said second fluid flow stream to thereby form a reaction product stream; and
 - an outlet port for allowing said reaction product stream to exit said junction device;
 - a second reaction zone downstream of said junction device where said plurality of reagent samples and said plurality of particles further mix and form a

plurality of reaction products, said second reaction zone communicating with said outlet port; and

means operatively connected to said outlet port and said second reaction zone for selectively analyzing said reaction product stream for said reaction products.

2. The microfluidic mixing apparatus of claim 1, wherein said first driving means comprises an autosampler.

3. The microfluidic mixing apparatus of claim 2, wherein said autosampler includes a probe and said microfluidic mixing apparatus includes a means for exposing a probe tip of said probe to a jet of gas to remove liquid from said probe tip.

4. The microfluidic mixing apparatus of claim 2, wherein said autosampler includes a probe having a conical tip.

5. The microfluidic mixing apparatus of claim 2, wherein said autosampler includes a hydrophobic probe.

6. The microfluidic mixing apparatus of claim 5, wherein said probe comprises a hydrophobic material.

7. The microfluidic mixing apparatus of claim 5, wherein said probe is coated with

a hydrophobic material.

8. The microfluidic mixing apparatus of claim 2, wherein said first driving means further comprises a first fluid flow stream peristaltic pump.

9. The microfluidic mixing apparatus of claim 8, wherein a portion of said fluid flow stream passing through said first fluid flow stream peristaltic pump is contained within a high speed multi-sample tube.

10. The microfluidic mixing apparatus of claim 8, wherein said first fluid flow stream peristaltic pump is located along said first fluid flow stream between said autosampler and said junction device.

11. The microfluidic mixing apparatus of claim 8, wherein said second driving means comprises a second fluid flow stream peristaltic pump.

12. The microfluidic mixing apparatus of claim 11, wherein a portion of said second fluid flow stream passing through said second fluid flow stream peristaltic pump is contained within a high speed multi-sample tube.

13. The microfluidic mixing apparatus of claim 11, wherein said first fluid flow stream peristaltic pump and said second fluid flow stream peristaltic pump comprise the same peristaltic pump.

14. The microfluidic mixing apparatus of claim 1, wherein said reaction product driving means comprises said first driving means and said second driving means.
15. The microfluidic mixing apparatus of claim 14, wherein said first driving means, said second driving means and said reaction product driving means comprises the same peristaltic pump.
16. The microfluidic mixing apparatus of claim 1, further comprising a first tubing for containing said first fluid flow stream, a second tubing for containing said second fluid flow stream and a reaction product tubing for containing said reaction product stream.
17. The microfluidic mixing apparatus of claim 16, wherein said microfluidic mixing apparatus includes a unibody flow apparatus comprising said first tubing, said second tubing, said reaction product tubing, and said junction device.
18. The microfluidic mixing apparatus of claim 16, wherein said first tubing comprises high speed multi-sample tubing.
19. The microfluidic mixing apparatus of claim 18, wherein said high speed multi-sample tubing comprises PVC tubing having an inner diameter about 0.005 to about 0.02 inches and a wall thickness of about 0.01 to about 0.03 inches.
20. The microfluidic mixing apparatus of claim 18, wherein said high speed multi-sample tubing comprises PVC tubing having an inner diameter about 0.01 inches and a

wall thickness of about 0.01 to about 0.03 inches.

21. The microfluidic mixing apparatus of claim 16, wherein said second tubing comprises high speed multi-sample tubing.

22. The microfluidic mixing apparatus of claim 21, wherein said high speed multi-sample tubing comprises PVC tubing having an inner diameter about 0.005 to about 0.02 inches and a wall thickness of about 0.01 to about 0.03 inches.

23. The microfluidic mixing apparatus of claim 21, wherein said high speed multi-sample tubing comprises PVC tubing having an inner diameter about 0.01 inches and a wall thickness of about 0.01 to about 0.03 inches.

24. The microfluidic mixing apparatus of claim 16, wherein said reaction product tubing comprises high-speed multi-sample tubing.

25. The microfluidic mixing apparatus of claim 24, wherein said high speed multi-sample tubing comprises PVC tubing having an inner diameter about 0.005 to about 0.02 inches and a wall thickness of about 0.01 to about 0.03 inches.

26. The microfluidic mixing apparatus of claim 24, wherein said high speed multi-sample tubing comprises PVC tubing having an inner diameter about 0.01 inches and a wall thickness of about 0.01 to about 0.03 inches.

27. The microfluidic mixing apparatus of claim 1, wherein said first inlet port, said

second inlet port and said outlet port each have an inner diameter about 0.005 to about 0.02 inches.

28. The microfluidic mixing apparatus of claim 1, wherein said first inlet port, said second inlet port and said outlet port each have an inner diameter about 0.01 inches.

29. The microfluidic mixing apparatus of claim 1, wherein said separation gas comprises air.

30. The microfluidic mixing apparatus of claim 1, wherein said plurality of reagent samples are homogenous.

31. The microfluidic mixing apparatus of claim 1, wherein said plurality of reagent samples are heterogeneous.

32. The microfluidic mixing apparatus of claim 1, wherein said particles comprise biomaterials.

33. The microfluidic mixing apparatus of claim 32, wherein said biomaterials are fluorescently tagged.

34. The microfluidic mixing apparatus of claim 1, further comprising a well plate including said plurality of respective source wells.

35. The microfluidic mixing apparatus of claim 34, wherein said well plate includes at least 60 source wells.
36. The microfluidic mixing apparatus of claim 34, wherein said well plate includes at least 72 source wells.
37. The microfluidic mixing apparatus of claim 34, wherein said well plate includes at least 96 source wells.
38. The microfluidic mixing apparatus of claim 34, wherein said well plate includes at least 384 source wells.
39. The microfluidic mixing apparatus of claim 34, wherein said well plate includes at least 1536 source wells.
40. The microfluidic mixing apparatus of claim 34, wherein said well plate includes wells having a conical shape.
41. The microfluidic mixing apparatus of claim 34, wherein said well plate is mounted in an inverted position.
42. The microfluidic mixing apparatus of claim 1, further comprising a means for injecting a buffer fluid between adjacent reagent samples in said first fluid flow stream.
43. The microfluidic mixing apparatus of claim 1, wherein at least one of said

plurality of reagent samples comprises a drug.

44. The microfluidic mixing apparatus of claim 1, wherein said junction device is Y-shaped.

45. The microfluidic mixing apparatus of claim 44, wherein the angle between any two of said first inlet port, said second inlet port and said outlet port is 120° .

46. The microfluidic mixing apparatus of claim 1, wherein said junction device is T-shaped.

47. The microfluidic mixing apparatus of claim 1, further comprising a first inlet tube connected to said first inlet port, a second inlet tube connected to said second inlet port and an outlet tube connected to said outlet port, wherein said first inlet tube and said first inlet port have the same inner diameter, wherein said second inlet tube and said second inlet port have the same inner diameter, and said outlet tube and said outlet port have the same inner diameter.

48. The microfluidic mixing apparatus of claim 47, wherein said first inlet port, said second inlet port and said outlet port each have the same interior diameter.

49. The microfluidic mixing apparatus of claim 47, wherein said first inlet port and said second inlet port have the same inner diameter and said outlet port has a different inner diameter from said first inlet port and said second inlet port.

50. The microfluidic mixing apparatus of claim 49, wherein said outlet port has a larger inner diameter than said first inlet port and said second inlet port.